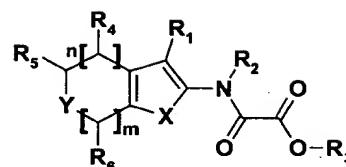


WHAT IS CLAIMED IS:

1. A compound of Formula 1

Sub
B1
5

Formula 1

wherein

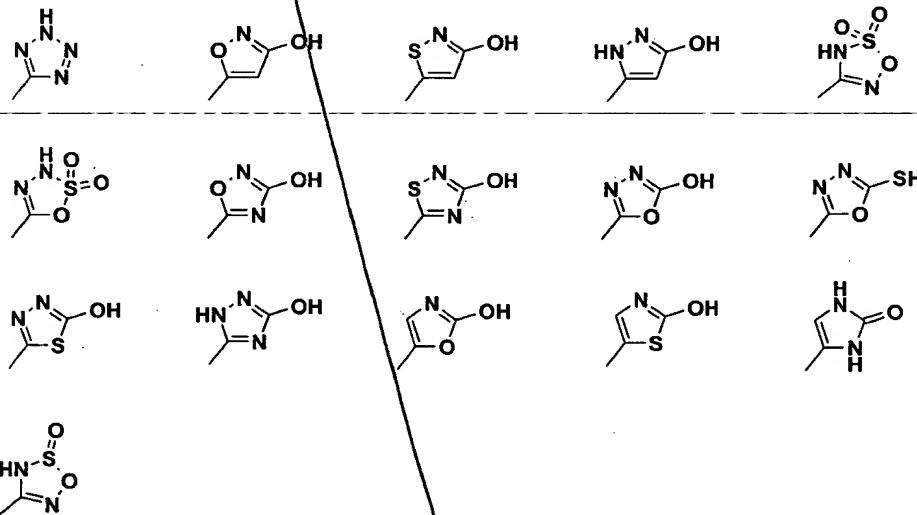
n is 0, 1 or 2;

10 m is 1 or 2;

X is S or O;

Y is O, S, SO or SO₂;R₁ is hydrogen or COOR₃, or R₁ is selected from the group consisting of the following 5-membered heterocycles:

15

R₂ is hydrogen, C₁-C₆alkyl, hydroxy or NR₇R₈;

20

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄, R₅ and R₆ are independently hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxy-carbonyl, aryloxycarbonyl, arylC₁-

5 C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, thio, C₁-C₆alkylthio, C₁-C₆alkylthioC₁-C₆alkyl, arylthio, arylC₁-C₆alkyl-thio, arylC₁-C₆alkylthioC₁-C₆alkyl, NR₈R₉, C₁-C₆alkylaminoC₁-C₆alkyl, aryl-C₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkyl-carbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-

10 C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxy, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkyl-carboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₁, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are 15 optionally substituted as defined in the section of definitions and R₁₁ is NR₇R₈, or C₁-C₆alkylNR₇R₈;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkyl-carboxy or arylC₁-

20 C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined in the section of definitions; or

R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sul-

25 phur, the ring system can optionally be substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, C₁-C₆alkyloxy, arylC₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino-C₁-C₆alkyl or NR₉R₁₀, wherein R₉ and R₁₀ are independently selected from hydro-

gen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-

C₆alkylcarbonyl, C₁-C₆-alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl

30 groups are optionally substituted as defined in the section of definitions; or

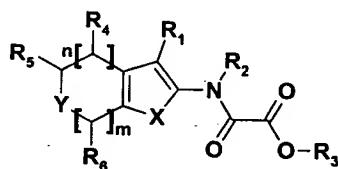
R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or

35 mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

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2. A compound of Formula 1



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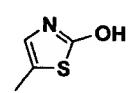
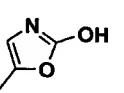
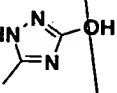
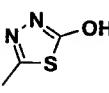
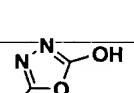
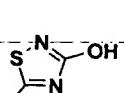
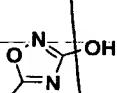
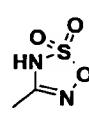
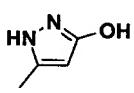
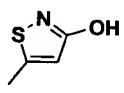
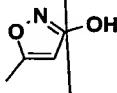
Formula 1

wherein

n is 0, 1 or 2;

m is 1 or 2;

10 X is S or O;

Y is O, S, SO or SO₂;R₁ is hydrogen or COOR₃, or R₁ is selected from the group consisting of the following 5-membered heterocycles:

15

R₂ is hydrogen, C₁-C₆alkyl, hydroxy or NR₇R₈;20 R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄, R₅ and R₆ are independently hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxy-carbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, 5 arylC₁-C₆alkyloxyC₁-C₆-alkyl, thio, C₁-C₆alkyl-thio, C₁-C₆alkylthioC₁-C₆alkyl, arylthio, arylC₁-C₆alkyl-thio, arylC₁-C₆alkylthioC₁-C₆alkyl, NR₈R₉, C₁-C₆alkylaminoC₁-C₆alkyl, aryl-C₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkyl-carbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆-alkylcarbonylC₁-C₆alkyl, C₁-C₆alkyl-carboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxy, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkyl-carboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonyl-aminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₁, arylC₁-C₆alkyl-carbonyl-amino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, or C₁-C₆alkyl-CONR₇R₈ wherein 10 the alkyl and aryl groups are optionally substituted and R₁₁ is NR₇R₈, or C₁-C₆alkylNR₇R₈;

15 R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted; or R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic cyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon 20 atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, the ring system can optionally be substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, C₁-C₆alkyloxy, arylC₁-C₆alkyloxy, C₁-C₆-alkyloxyC₁-C₆alkyl, C₁-C₆alkylamino-C₁-C₆alkyl or NR₉R₁₀, wherein R₉ and R₁₀ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted; or 25 R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

30 or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form.

3. A compound according to claim 2 wherein X is sulphur.

35 4. A compound according to claim 3 wherein R₁ is COOR₃ and R₂ is hydrogen.

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5. A compound according to claim 4 wherein n and m are 1.
6. A compound according to claim 5 wherein Y is oxygen.
- 5
7. A compound according to claim 4 wherein R_5 is C_1-C_6 alkylNR₇R₈.
8. A compound according to claim 7 wherein R_4 and R_6 are hydrogen.
- 10 9. A compound according to claim 3 wherein R_1 is 5-tetrazolyl, R_2 is hydrogen, R_5 is C_1-C_6 alkylNR₇R₈ and Y is oxygen.
10. A compound according to claim 3 wherein R_1 is 5-tetrazolyl, R_2 is hydrogen, R_6 is C_1-C_6 alkylNR₇R₈ and Y is oxygen.
- 15 11. A compound according to claim 6 wherein R_6 is C_1-C_6 alkylNR₇R₈.
12. A compound according to claim 11 wherein R_4 and R_5 are hydrogen.
- 20 13. A compound according to claim 11 wherein R_7 and R_8 together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic cyclic, bicyclic or tricyclic ring system.
14. A compound according to claim 13 wherein the ring system is 1,3-dihydro-
- 25 15. A compound according to claim 13 wherein the ring system is 1,3-dihydrobenzo[d]isothiazolyl, substituted with 2 or 3 oxo groups at the atom positions adjacent to the nitrogen atom.
16. A compound according to claim 1 wherein X is sulphur.
- 30 17. A compound according to claim 1 wherein R_1 is COOR₃ and R_2 is hydrogen.
18. A compound according to claim 1 wherein Y is oxygen.

19. A compound according to claim 1 wherein R_5 is C_1 - C_6 alkylNR₇R₈.

20. A compound according to claim 1 wherein R_4 and R_6 are hydrogen.

5 21. A compound according to claim 1 wherein R_1 is 5-tetrazolyl, R_2 is hydrogen, R_5 is C_1 - C_6 alkylNR₇R₈ and Y is oxygen.

22. A compound according to claim 1 wherein R_1 is 5-tetrazolyl, R_2 is hydrogen, R_6 is C_1 - C_6 alkylNR₇R₈ and Y is oxygen.

10

23. A compound according to claim 1 wherein R_6 is C_1 - C_6 alkylNR₇R₈.

24. A compound according to claim 1 wherein R_4 and R_5 are hydrogen.

15 25. A compound according to claim 1 wherein R_7 and R_8 together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system.

26. A compound according to claim 1 wherein the ring system is 1,3-dihydro-

20 benzo[d]isothiazolyl, substituted with 2 or 3 oxo groups at the atom positions adjacent to the nitrogen atom.

27. A compound according to claim 1 wherein the ring system is 1,3-dihydro-isoindol, substituted with 1 or 2 oxo groups at the atom positions adjacent to the nitrogen atom.

25

28. A compound according to claim 1 wherein the ring system is optionally substituted with hydroxy, nitro, methoxy, benzyloxy, fluoro, chloro, $CH_3CH_2CH_2NHC(O)-$ or $CH_3C(O)NH-$.

30 29. A compound according to claim 1 wherein R_7 and R_8 together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic cyclic, bicyclic or tricyclic ring system.

30. A compound according to claim 1 wherein the ring system is 1,3-dihydro-isoindol, substituted with 1 or 2 oxo groups at the atom positions adjacent to the nitrogen atom.

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31. A compound according to claim 1 wherein the ring system is optionally substituted with hydroxy, nitro, methoxy, benzyloxy, fluoro, chloro, $\text{CH}_3\text{CH}_2\text{CH}_2\text{NHC(O)-}$ or $\text{CH}_3\text{C(O)NH-}$.

32. A compound according to claim 1 wherein the ring system is thiazolidin-2,4-dione.

5

33. A compound according to claim 1 wherein the ring system is 5-arylidene-thiazolidin-2,4-dione.

10

34. A compound according to claim 1 wherein the aryl group is phenyl optionally substituted with methoxy or $\text{CH}_3\text{C(O)-}$.

15

35. A compound according to claim 1 wherein the aryl group is pyridyl.

36. A compound according to claim 1 wherein the aryl group is 4(5)-imidazolyl.

20

37. A compound according to claim 1 wherein the ring system is 5-(aryl-methyl)-thiazolidin-2,4-dione.

25

38. A compound according to claim 1 wherein the aryl group is pyridyl.

39. A compound according to claim 1 wherein R_7 is hydrogen and R_8 is $-\text{C(O)-aryl}$.

40. A compound according to claim 1 wherein the aryl group is phenyl optionally substituted as defined for optionally substituted aryl.

41. A compound according to claim 1 wherein the aryl group is benzo[1,3]dioxole.

42. A compound according to claim 1 wherein R_7 is hydrogen and R_8 is $-\text{C(O)-C}_1\text{-C}_6\text{alkylaryl}$.

30

43. A compound according to claim 1 wherein the aryl group is phenyl optionally substituted as defined for optionally substituted aryl.

44. A compound according to claim 1 wherein R_5 is $-\text{C(O)NR}_7\text{R}_8$.

35

45. A compound according to claim 1 wherein R_7 is hydrogen and R_8 is aryl.

46. A compound according to claim 1 wherein R₇ is hydrogen and R₈ is C₁-C₆alkylaryl.

47. A compound according to claim 1 wherein R₆ is -C(O)NR₇R₈.

5 48. A compound according to claim 1 wherein R₇ is hydrogen and R₈ is aryl.

49. A compound according to claim 1 wherein R₇ is hydrogen and R₈ is C₁-C₆alkylaryl.

10 50. A compound according to claim 1 wherein the ring system is pyrrolo[3,4-c]pyridine-1,3-dione.

51. A compound according to claim 1 wherein the ring system is pyrrolo[3,4-b]pyridine-5,7-dione.

15 52. A compound according to claim 1 wherein the ring system is pyrrolo[3,4-b]pyrazine-5,7-dione.

53. A compound according to claim 1 wherein the ring system is pyrrolo[3,4-c]pyridine-1,3-dione.

20 54. A compound according to claim 1 wherein R₆ is arylaminocarbonylaminoC₁-C₆alkyl.

55. A compound according to claim 1 wherein the aryl group is phenyl optionally substituted as defined for optionally substituted aryl.

25 56. A compound according to claim 1 wherein R₆ is aryloxyC₁-C₆alkyl.

57. A compound according to claim 1 wherein the aryl group is 1,1-dioxo-benzo[d]isothiazol-3-yl.

30 58. A compound according to claim 1 wherein the aryl group is 1,1-dioxo-5-phenyl-isothiazol-3-yl.

59. A compound according to claim 1 wherein the ring system is 6-chloro-1,1,3-trioxo-2,3-dihydro-4H-thieno[3,2-e]-1,2,4-thiadiazin-2-yl.

60. A compound according to claim 1 wherein the aryl group is 6-chloro-1,1-dioxo-2,3-dihydro-4H-thieno[3,2-e]-1,2,4-thiadiazin-3-yl.

5 61. A compound according to claim 1 wherein R₅ is aryloxyC₁-C₆alkyl.

62. A compound according to claim 1 wherein the aryl group is 1,1-dioxo-5-phenyl-isothiazol-3-yl.

10 63. A compound according to claim 1 wherein the ring system is 1,1,3-trioxo-5-phenyl-isothiazol-2-yl.

15 64. A compound according to claim 1 wherein the ring system is 5-benzyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-yl.

65. A compound according to claim 1 wherein the ring system is 5-ethyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-yl.

20 66. A compound according to claim 1 wherein R₇ is hydrogen and R₈ is aryIC₁-C₆alkyl, wherein the aryl and alkyl groups are optionally substituted as defined for optionally substituted alkyl and optionally substituted aryl in the section of definitions.

67. A compound according to claim 1 wherein the aryl group is benzo[1,3]dioxol-5-yl.

25 68. A compound according to claim 1 wherein the aryl group is 5-methoxy-2-methyl-1H-indol-3-yl.

69. A compound according to claim 1 selected from the following:
2-(Oxalyl-amino)-7-(1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;
or a pharmaceutically acceptable salt thereof.

30 70. A compound according to claim 2 selected from the following:

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5-(4-Chloro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4,5,6,7-Tetrachloro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5 5-(5-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Benzylxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

10 5-(4-Fluoro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,3-Dioxo-1,3-dihydro-benzo[f]isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

15 5-(5-Acetylamino-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Acetylamino-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyrazin-6-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

20 7-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

25 5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-c]pyridin-6-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Nitro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

30 5-(4-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Nitro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

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5-(4-(4-Chloro-phenylsulfanyl)-6-methyl-1,3-dioxo-1,3-dihydro-pyrrolo[3,4-c]pyridin-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(3-Imidazol-1-yl-2,5-dioxo-pyrrolidin-1-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5 Oxalic acid 3-carboxy-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl ester methyl;

Oxalic acid (3-carboxy-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl) ester;

7-Hydroxymethyl-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(2,4-Dioxo-thiazolidin-3-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

10 10

7-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl oxymethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(4-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

15 15

5-(5-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5,7-Dioxo-5,7-dihydro-[1,3]dioxolo[4,5-f]isoindol-6-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(((Benzo[1,3]dioxole-5-carbonyl)amino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

20 20

7-(3-(2,4-Dimethoxy-phenyl)ureidomethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxaryl-amino)-5-phenylcarbamoyl-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-Benzylcarbamoyl-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

25 25

2-(Oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3,7-dicarboxylic acid 7-ethyl ester

7-Benzylcarbamoyl-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-(4-Methanesulfonyl-phenyl)-acetylamino)-methyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

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2-((3-Carboxy-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl)-carbamoyl)nicotinic acid;

7-(2,4-Dioxo-5-pyridin-2-ylmethylene-thiazolidin-3-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(2,4-Dioxo-5-pyridin-2-ylmethyl-thiazolidin-3-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(4-Methoxy-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(4-Acetylamino-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5 7-(5-(3,5-Dimethoxy-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-[5-(1H-Imidazol-4(5)-ylmethylene)-2,4-dioxo-thiazolidin-3-ylmethyl]-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,3-Dioxo-4,7-epoxido-1,3,4,5,6,7-hexahydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

10 7-((2R)-2-Amino-3-phenyl-propionylamino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

15 7-((2-Acetylamino-3-methyl-butyrylamino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxaryl-amino)-7-(1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

or a pharmaceutically acceptable salt thereof.

20

71. A compound according to claim 1 selected from the following:

2-(Oxaryl-amino)-7-(1,1,3-trioxo-1H-benzo[d]isothiazol-3-yloxomethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

25 2-(Oxaryl-amino)-7-(3-oxo-3H-benzo[d]isoxazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxaryl-amino)-7-(1,1,3-trioxo-5-phenyl-1,3-dihydro-isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

30 7-(1,1-Dioxo-5-phenyl-1H-isothiazol-3-yloxymethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxaryl-amino)-5-(1,1,3-trioxo-5-phenyl-1,3-dihydro-isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

35 5-(1,1-Dioxo-5-phenyl-1H-isothiazol-3-yloxymethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(6-Chloro-1,1,3-trioxo-2,3-dihydro-4H-thieno[3,2-e]-1,2,4-thiadiazin-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

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5-(6-Chloro-1,1-dioxo-4*H*-thieno[3,2-e]-1,2,4-thiadiazine-3-yloxymethyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

7-(1,3-Dioxo-1,3-dihydro-benzo[d]isothiazol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

5 5-(1,3-Dioxo-1,3-dihydro-benzo[d]isothiazol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Benzyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Ethyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxaryl-amino)-7-(1-oxo-1,3-dihydro-isoindol-2-ylmethyl)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxaryl-amino)-5-(2,2,2-trifluoro-acetoxymethyl)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

15 5-((Benzo[1,3]dioxol-5-ylmethyl)-amino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

5-((2-Methoxy-benzylamino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

20 5-((2-Benzo[1,3]dioxol-5-yl-acetylamino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

5-(((5-Methoxy-2-methyl-1*H*-indol-3-carbonyl)amino)methyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,3-Dioxo-5-propylcarbamoyl-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxaryl-amino)-4,7-dihydro-5*H*-thieno[2,3-c]pyran-3-carboxylic acid;

25 or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

72. Compounds according to claim 1 which act as inhibitors of Protein Tyrosine Phosphatases.

30 73. A pharmaceutical composition comprising an effective amount of a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents.

74. A pharmaceutical composition suitable for treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising an effective amount of a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents.

5

75. A pharmaceutical composition suitable for treating immune dysfunctions including autoimmunity, diseases with dysfunctions of the coagulation system, allergic diseases, osteoporosis, proliferative disorders including cancer and psoriasis, diseases with decreased or increased synthesis or effects of growth hormone, diseases with decreased or increased synthesis of hormones or cytokines that regulate the release of/or response to growth hormone, diseases of the brain including Alzheimer's disease and schizophrenia, and infectious diseases comprising an effective amount of a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents.

10

15 76. The pharmaceutical composition of claim 73 in the form of an oral dosage unit or parenteral dosage unit.

20

77. The pharmaceutical composition of claim 73 wherein the compound is administered as a dose in a range from about 0.05 to 1000 mg.

25

78. A compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for therapeutical use.

30

79. A compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for therapeutical use in the treatment or preventing of type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity.

35

80. A compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for therapeutical use in the treatment or preventing of immune dysfunctions including autoimmunity, diseases with dysfunctions of the coagulation system, allergic diseases, osteoporosis, proliferative disorders including cancer

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and psoriasis, diseases with decreased or increased synthesis or effects of growth hormone, diseases with decreased or increased synthesis of hormones or cytokines that regulate the release of/or response to growth hormone, diseases of the brain including Alzheimer's disease and schizophrenia, and infectious diseases.

5

81. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form as a medicament.

10

82. The use of a compound according to claim 1 for preparing a medicament.

83. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for the preparation of a medicament suitable for the treatment or preventing of type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity.

15

84. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for the preparation of a medicament suitable for the treatment or preventing of immune dysfunctions including autoimmunity, diseases with dysfunctions of the coagulation system, allergic diseases, osteoporosis, proliferative disorders including cancer and psoriasis, diseases with decreased or increased synthesis or effects of growth hormone, diseases with decreased or increased synthesis of hormones or cytokines that regulate the release of/or response to growth hormone, diseases of the brain including Alzheimer's disease and schizophrenia, and infectious diseases.

25

85. A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity, comprising: administering to a subject in need thereof an effective amount of a compound of claim 1.

30

86. A method of treating immune dysfunctions including autoimmunity, diseases with dysfunctions of the coagulation system, allergic diseases, osteoporosis, proliferative disorders including cancer and psoriasis, diseases with decreased or increased synthesis or

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effects of growth hormone, diseases with decreased or increased synthesis of hormones or cytokines that regulate the release of/or response to growth hormone, diseases of the brain including Alzheimer's disease and schizophrenia, and infectious diseases comprising administering to a subject in need thereof an effective amount of a compound of claim 1.

5

87. A process for the manufacture of a medicament, particular to be used in the treatment or prevention of type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity, which process comprises bringing a compound according to claim 1 or a pharmaceutically acceptable salt thereof into a galenic dosage form.

10

88. A process for the manufacture of a medicament, particular to be used in the treatment or prevention of immune dysfunctions including autoimmunity, diseases with dysfunctions of the coagulation system, allergic diseases, osteoporosis, proliferative disorders including cancer and psoriasis, diseases with decreased or increased synthesis or effects of growth hormone,

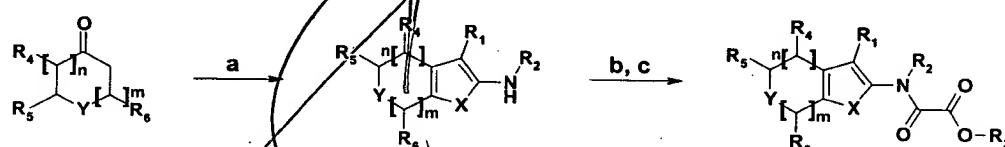
15 diseases with decreased or increased synthesis of hormones or cytokines that regulate the release of/or response to growth hormone, diseases of the brain including Alzheimer's disease and schizophrenia, and infectious diseases, which process comprises bringing a compound according to claim 1 or a pharmaceutically acceptable salt thereof into a galenic dosage form.

20

89. Any novel feature or combination of features as described herein.

90. A method for preparing a compound of Formula 1, comprising:

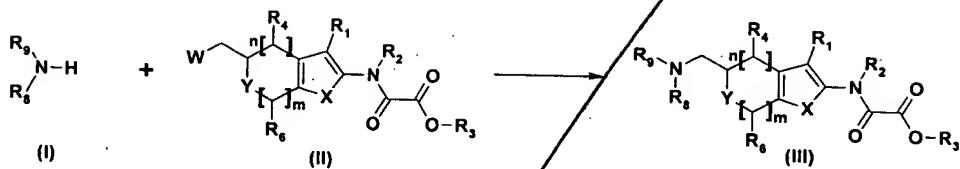
25 A)



a) $\text{NCCH}_2\text{COOR}_3$, sulphur, morpholine or triethylamine, EtOH; b) R_3OCOCO imidazole, THF;
c) 25 % TFA/CH₂Cl₂; wherein n, m, X, Y, R₁, R₂, R₃, R₄, R₅, and R₆ are defined in claim 1;

30

B)

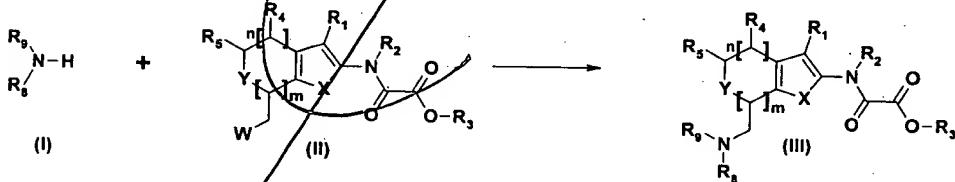


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allowing an amine (I) and a substituted oxalylamide (II) to react under basic conditions (e.g. K_2CO_3 , in N,N -dimethylformamide or methyl ethyl ketone) or under Mitsunobu conditions (Oyo Mitsunobu, *Synthesis*, (1981) 1-28) to yield (III) wherein W is OH , OSO_2Me or halo, and n , m , X , Y , R_1 , R_2 , R_3 , R_4 , R_6 , R_8 and R_9 are defined in claim 1;

10

c)



15 allowing an amine (I) and a substituted oxalylamide (II) to react under basic conditions (e.g. K_2CO_3 , in N,N -dimethylformamide or methylethylketone) or under Mitsunobu conditions (Oyo Mitsunobu, *Synthesis*, (1981) 1-28) to yield (III) wherein W is OH, OSO_2Me or halo, and n, m, X, Y, R_1 , R_2 , R_3 , R_4 , R_5 , R_8 and R_9 are defined in claim 1.

20 91. A pharmaceutical composition comprising an effective amount of a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitiser, such as a thiazolidinedione eg. troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione or a pharmaceutically acceptable salt thereof, preferably the potassium salt, or (-) 25 3-[4-[2-Phenoxyazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof, preferably the arginine salt.

92. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of

optical isomers, including a racemic mixture, or any tautomeric form and an insulin sensitizer, such as a thiazolidinedione eg. troglitazone, cigitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione or a pharmaceutically acceptable salt thereof, preferably the potassium salt, or (-) 3-[4-[2-

5 Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof, preferably the arginine salt for the preparation of a medicament suitable for the treatment or preventing of type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity.

10 93. A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 1 and an insulin sensitizer, such as a thiazolidinedione eg. troglitazone, cigitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione or a pharmaceutically acceptable salt thereof, preferably the potassium salt, or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof, preferably the arginine salt to said subject.

15 94. A pharmaceutical composition comprising an effective amount of a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells, such as repaglinide.

20 95. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form and an agent stimulating insulin release from β cells such as repaglinide for the preparation of a medicament suitable for the treatment or preventing of type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity.

25 30 96. A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound according to claim 1 and an agent stimulating insulin release from β cells such as repaglinide.

97. A pharmaceutical composition comprising a compound of claim 1 together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent such as orlistat.

5 98. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form and an and an antiobesity agent such as orlistat for the preparation of a medicament suitable for the treatment or preventing of type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity.

99. A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 1 and an antiobesity agent such as orlistat.